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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,047	12/06/2001	Theodora Ross	UM-06692	6232

7590 05/05/2006

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/05/2006

- - - - Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,047	ROSS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-27,29,36,84-86,91-93 and 95* is/are pending in the application.

4a) Of the above claim(s) *84-86 and 91-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,29,36 and 95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The Amendment filed on 3/22/2006 in response to the previous Final Office Action (1/26/2006) is acknowledged and has been entered. The Finality of the previous office action has been withdrawn upon reconsideration.

Claims 24-27, 29, 36, 84-86, 91-93 and 95 are currently pending.

Claims 84-86 and 91-93 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 24-27, 29, 36 and 95 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

New Rejections necessitated upon reconsideration:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-27, 29, 36 and 95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands

states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims read on a method of characterizing cancer in a subject comprising: (a) providing a sample from a subject, wherein the subject has been diagnosed with prostate cancer; and (b) characterizing said sample by detecting the presence or absence or HIP1 in said sample with a reagent configured to detect a HIP1 nucleic acid having the nucleic acid sequence of SEQ ID NO: 1, wherein said presence or absence of HIP1 in said sample is indicative of one or more properties of cancer selected from the group consisting of risk of prostate specific antigen failure, risk of cancer metastasizing, risk of cancer reoccurring, and stage of cancer. Thus, it appears that HIP1 in prostate tissues can be used as a marker for assessing the risk of prostate specific antigen failure, the risk of prostate cancer metastasizing, the risk of prostate cancer reoccurring or assessing the state of prostate cancer.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn a method of characterizing prostate cancer by measuring the absence or presence of HIP1 in a sample, wherein the absence or presence of HIP1 is indicative of prostate specific failure, the risk of prostate cancer metastasizing, the risk of prostate cancer reoccurring or the stage of cancer. The specification teaches (page 4, lines 9-12) that HIP1 may be utilized in a method for characterizing prostate tissue in a subject, wherein the presence or absence of HIP1 characterizes the tissue sample. For example, the specification teaches that HIP1 expression in individual patients reveals that there

were progressively higher frequencies of HIP1 expression in benign, PIN, PCA and metastatic case. Conversely, there were progressively lower frequencies of the lack of HIP1 expression among the same (page 65, lines 25-28 and Figure 4a). Moreover, the specification teaches the clinical implications associated with HIP1 expression, wherein patients with tumors which did not stain for HIP1 expression did not develop a PSA recurrence (page 66, lines 5-11 and page 67, Table 1). In addition, the specification teaches that there is a survival advantage of PCa patients with tumors that had no HIP1 expression, wherein all patients that lacked HIP1 expression survived 67 months without evidence of recurrence as compared to 28% of the patients whose tumors expressed HIP1 died of prostate cancer (page 66, lines 17-26 and Figure 4b). Thus, while the specification teaches that in some instances there is a correlation between HIP1 expression and prostate cancer, the specification does not appear to provide a nexus between the presence or absence of HIP1 in prostate tissues and the patients risk of prostate specific antigen failure, the risk of prostate cancer metastasizing, the risk of prostate cancer reoccurring or assessing the state of prostate cancer. For example, while the specification (page 65, lines 28-31) teaches the presence of HIP1 expression correlated with the ordinal categories of benign vs. PIN vs. PCa vs. Metastatic, the specification appears to be silent on an "amount" of HIP1 which can be used to differentiate the stage of cancer because the results shown in Figure 4a shows the frequency (% cases) of HIP1 expression and not a differentiating amount.

Therefore, the teachings above do not clearly indicate whether or not HIP1 is indicative of the cancerous state in prostate cells. In other words, what may be "preferable" in the lab is only suggestive and does not qualify as a reasonable expectation of success, especially in a highly unpredictable art such as determining the risk of cancer. For example, Tockman *et al* (Cancer Res., 1992, 52:2711s-2718s, *of record*) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Although, the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders such as prostate cancer. Tockman *et al* teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added)

can be used for population screening (p. 2713s, col. 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). In addition, Slamon et al. (Science Vol. 235, January 1987, pages 177-182, *of record*) teach other essential factors that are known to be important in the prognosis of breast cancer in individual patients such as size of the primary tumor, stage of the disease at diagnosis, hormonal receptor status, and number of axillary lymph nodes involved with disease (page 178, 1st column, 2nd paragraph). Such data are critical to assessing actuarial curves for relapse (Figure 3), and for comparing disease-free survival and overall survival to prognostic factors (Table 4).

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Therefore, No claim is allowed.

Conclusion

The closest prior art to the instantly claimed invention is Chen et al. (US 6,794,501) whom teaches a method of diagnosing colon cancer is a subject comprising obtaining a biological sample from a subject and determining the expression of a cancer-associated nucleic acid molecule that appears to be 60% identical to the instantly claimed nucleic acid of SEQ ID NO: 1. However, Chen et al. do not teach or suggest that the nucleic acid can be used to determine the of risk of prostate specific antigen failure, risk of cancer metastasizing, risk of cancer reoccurring, and stage of cancer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER